Self guided Tour

REAXYS MEDICINAL CHEMISTRY

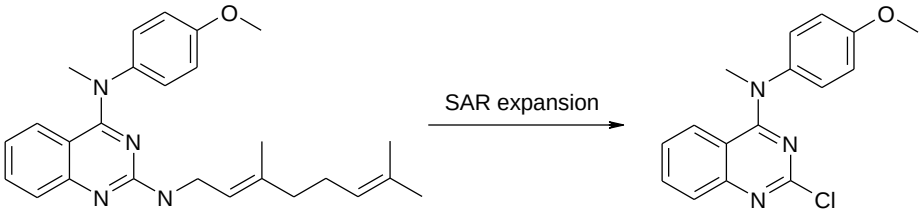
“WHAT IS KNOWN ABOUT MY SUBSTANCE OF INTEREST?”

http://beta.reaxys.com

WHAT IS KNOWN ABOUT MY SUBSTANCE OF INTEREST?

1.1 Scenario

An Apoptosis inducer 'chemotype' from a cell- and caspase-based apoptosis high-throughput screening was found (Compound 1). A structure activity relationship expansion lead to compound 2 (Schema1)



HTS hit
Compound 1

Compound 2

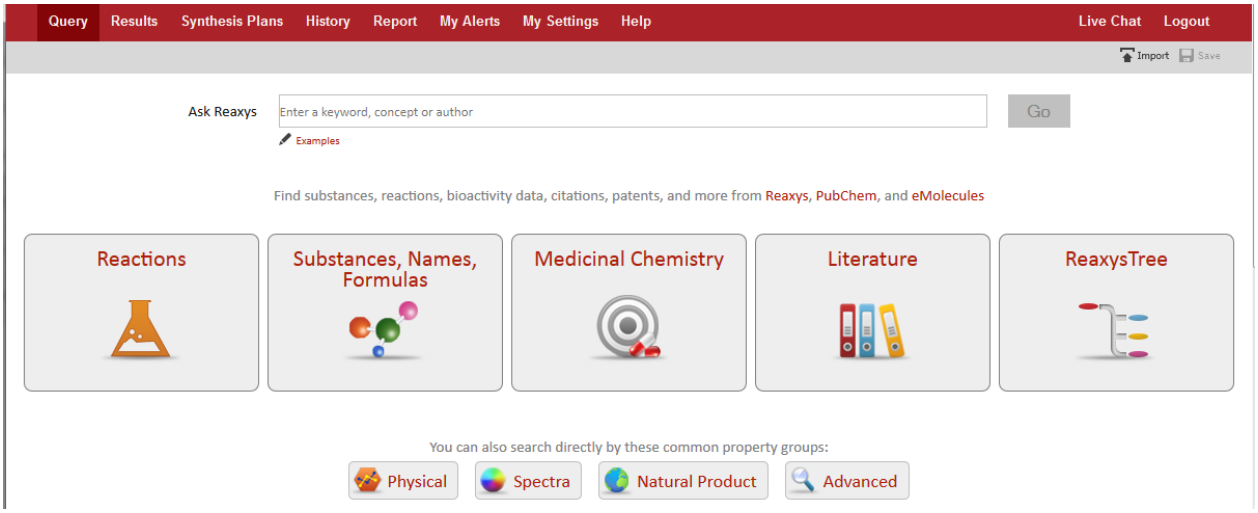
Figure 1 : Apotosis inducer : From HTS hit to new chemotype

What is known about this chemotype/template (Compound 2) in Reaxys Medicinal Chemistry?

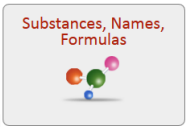
1.2 Overview

Step no.	Steps and description	Action
1	Search By Substances	Click on substance button
2	Draw your Substance	Use Marvin Sketch and draw structure
3	Search by Exact structure (default)	Click on Search Substances
4	"Substance Report" will display corresponding bioactivities	View default tab 'Substance Report'
5	"Bioactivity" link will display details on bioactivity categories	Check 'Bioactivity' link
6	Click on Bioactivity categories, it will display more details (biological results)	Check the three Bioactivity categories (In vivo, Pharmacokinetics, Toxicity)
7	Click on the bioactivities tab, it will display Substance and corresponding Targets (default view)	Click on 'Bioactivities' tab
8	Click on Axis values to change the heatmap view (cell lines instead of targets)	Click on Target X axis and change target to Cell lines in the popup
9	Click the Targets Tab	Click on 'Targets' tab
10	Click Show details in the target tab to know more about (Bioassays and cells lines)	Click on 'Show details' & Associated links under 'Show details'

1.3 Step by step

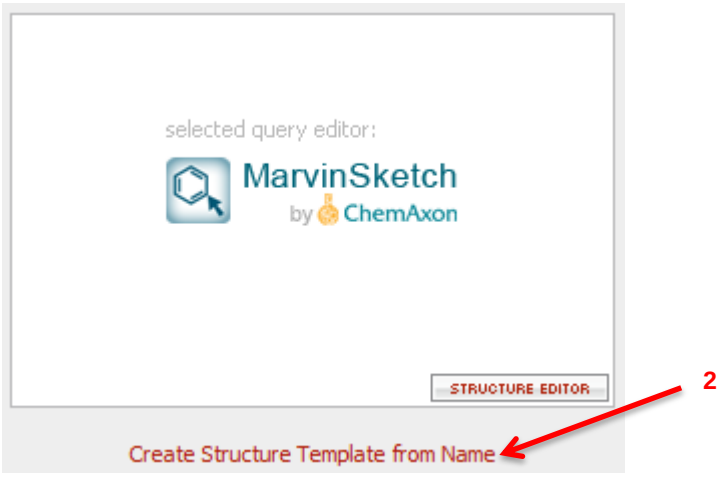


Step 1 Search By substances and Chemical drawing

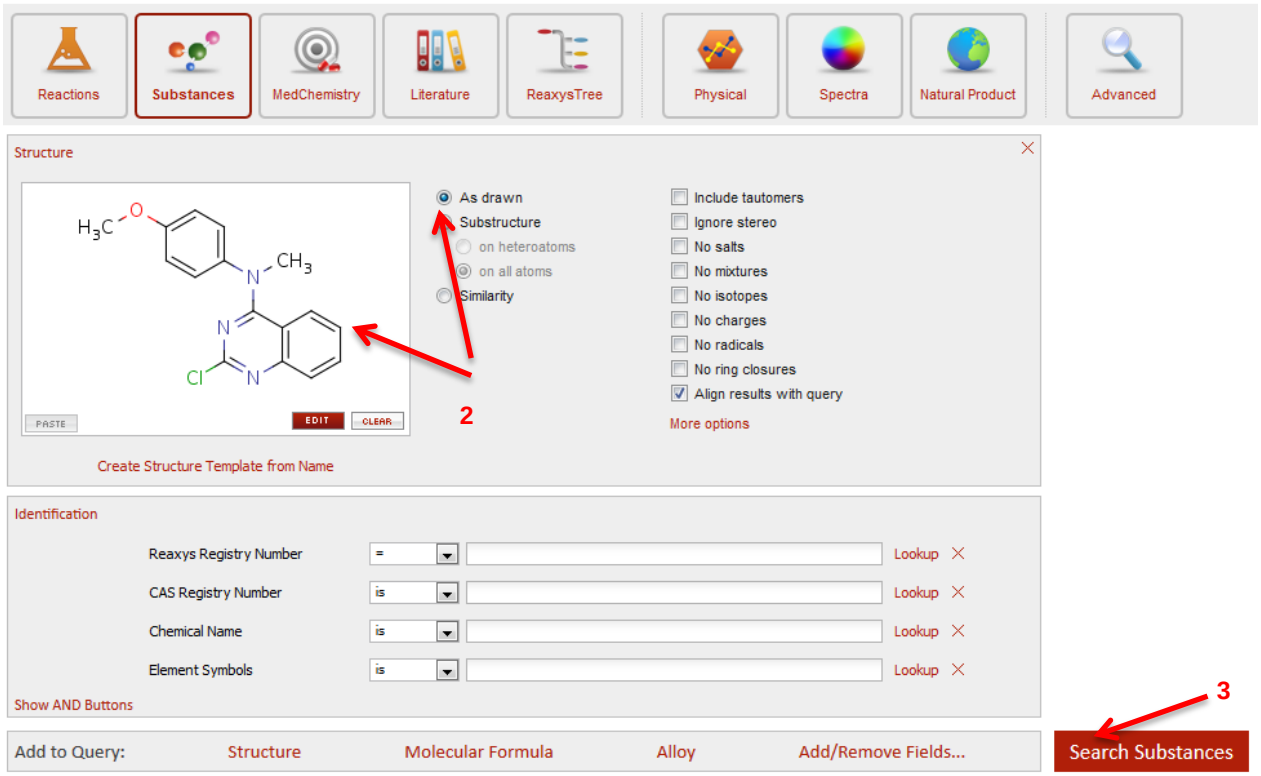
Step	Action	Comment
1	Click on Substances, Names and Formulas Button 	A new query Page dedicated to Substance will appear where you will be able to draw Compound 2
2	Draw the chemical compound 2 or copy Smile (See remark below) and paste the smile and Select As Drawn in the option on the right	Don't forget to transfer the query before closing the sketcher

<u>Remark :</u> In order to save time for drawing the compound use the "Create structure Template for Name" and paste the following Smile.

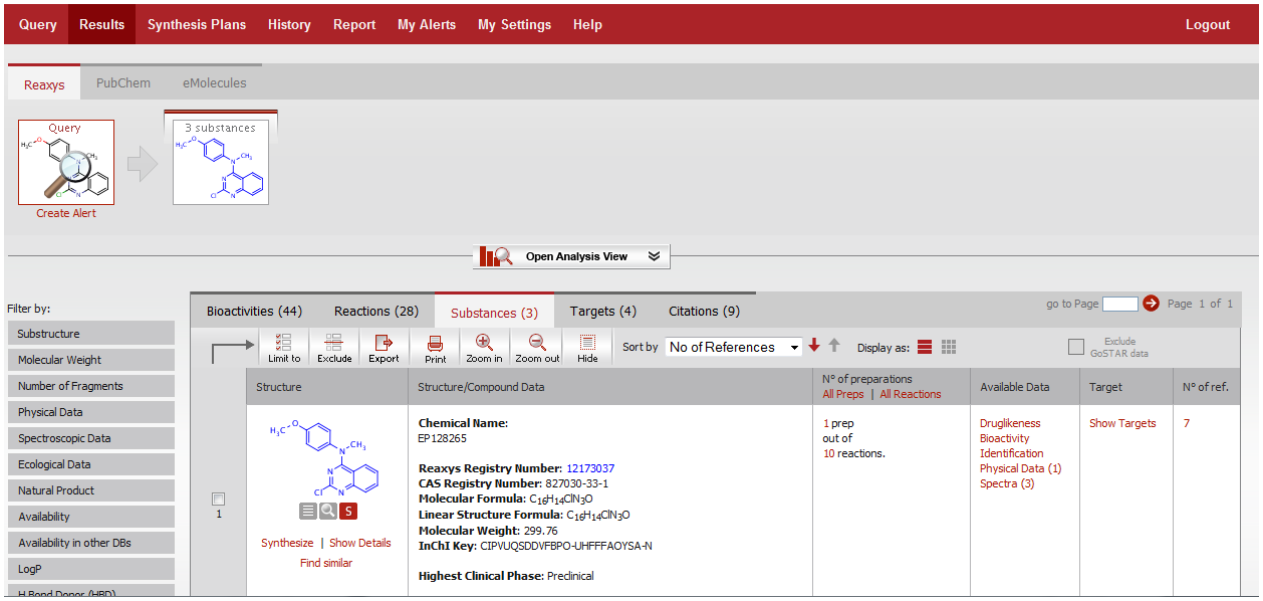
Smile : COC1=CC=C(C=C1)N(C)C1=NC(Cl)=NC2=C1C=CC=C2



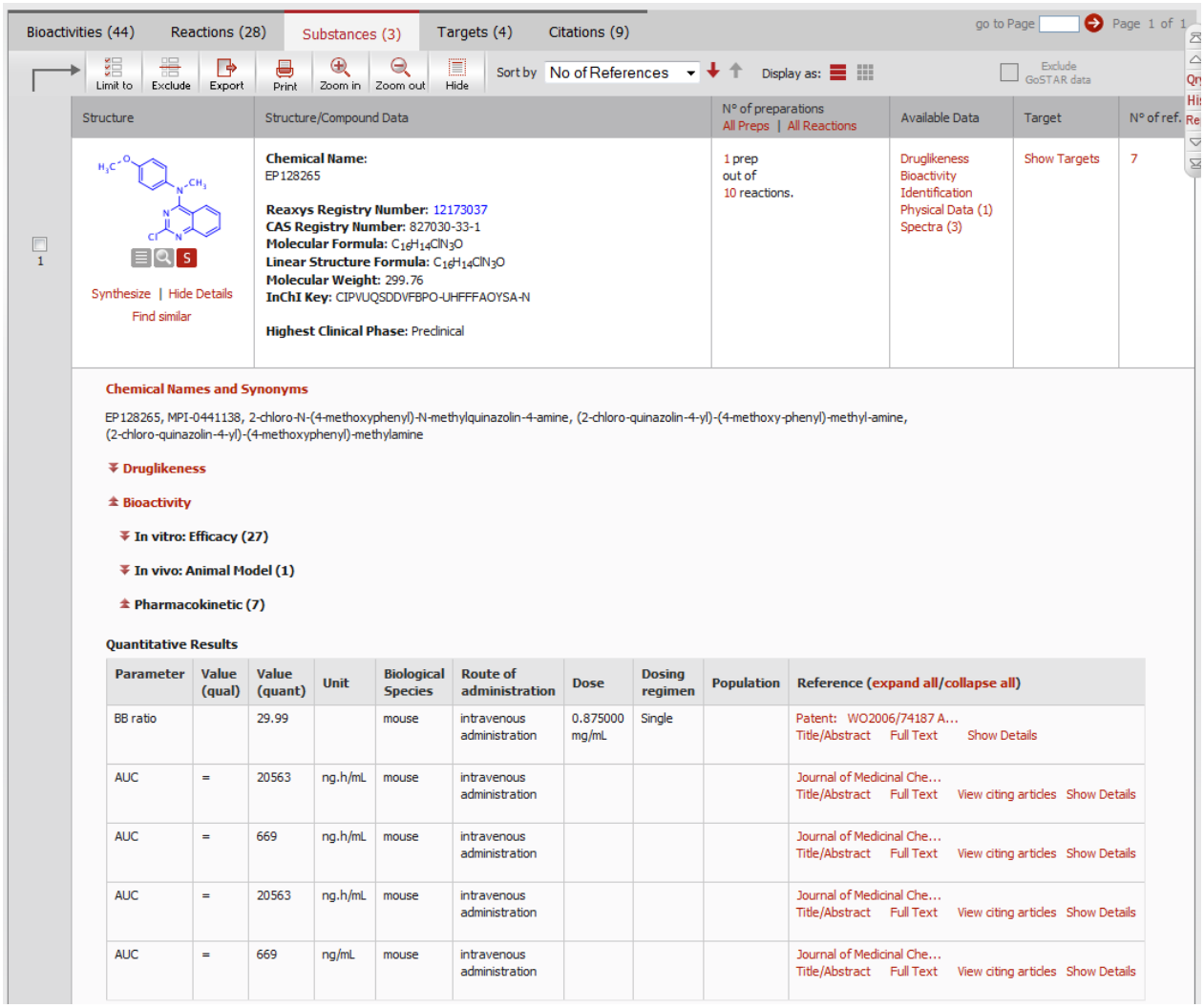
Step 2 : Search by Exact structure



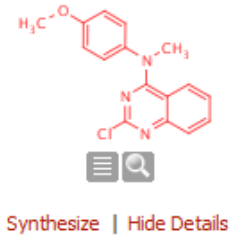
Step 3: Found Bioactivities of compound 2



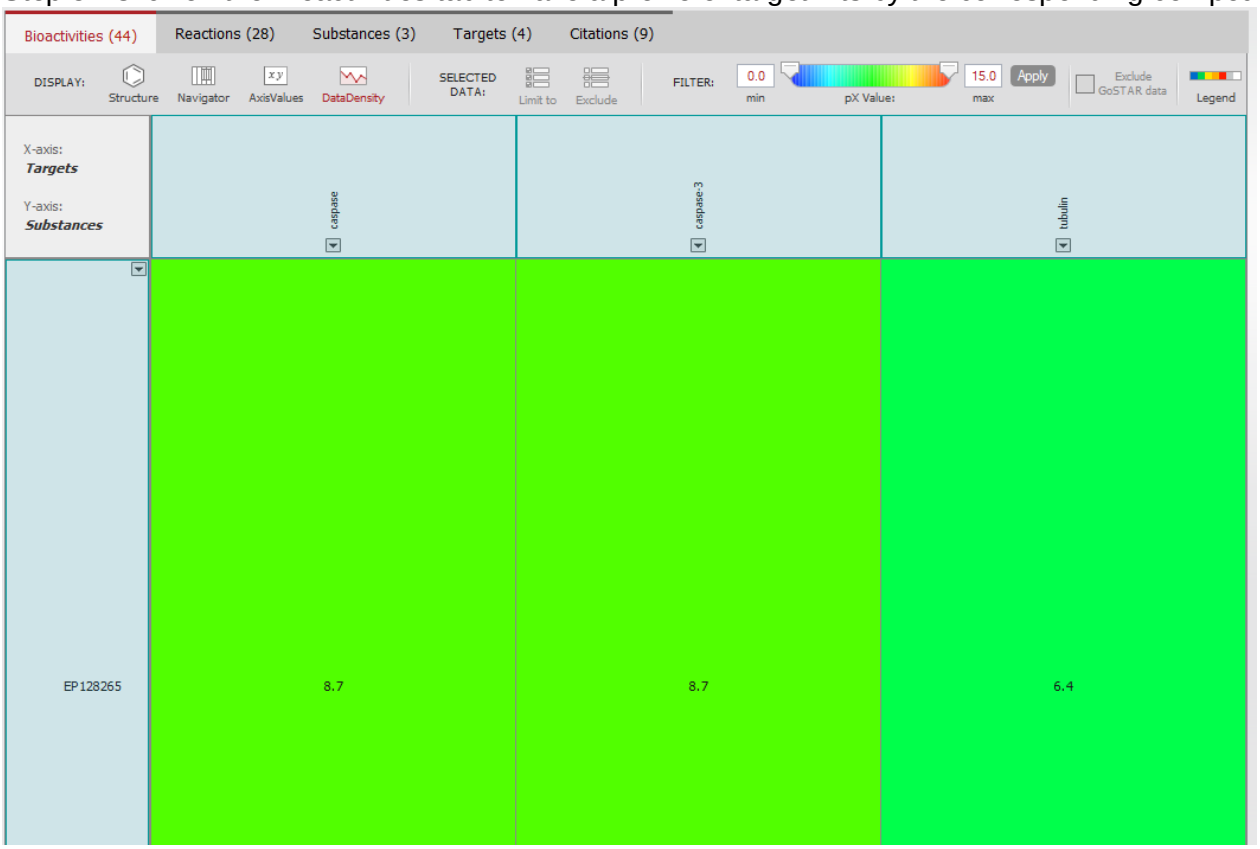
Step 4: Click on Bioactivity to display all the available bioactivities by Categories



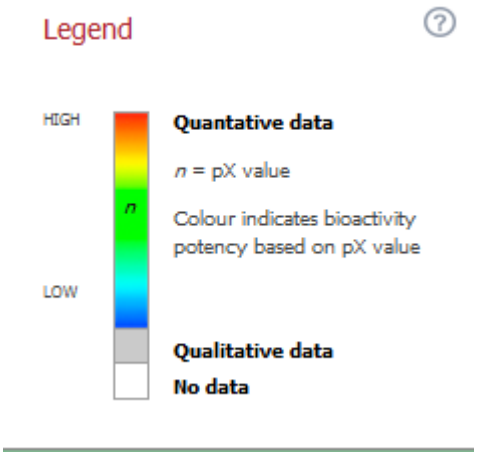
Remark : The Hide Details Link will collapse all the bioactivity details



Step 5 : Click on the Bioactivities tab to have a profile of target hits by the corresponding compound

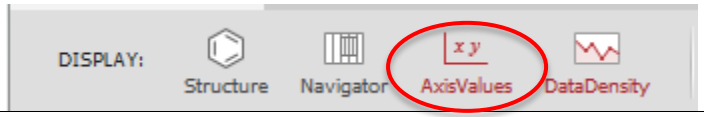
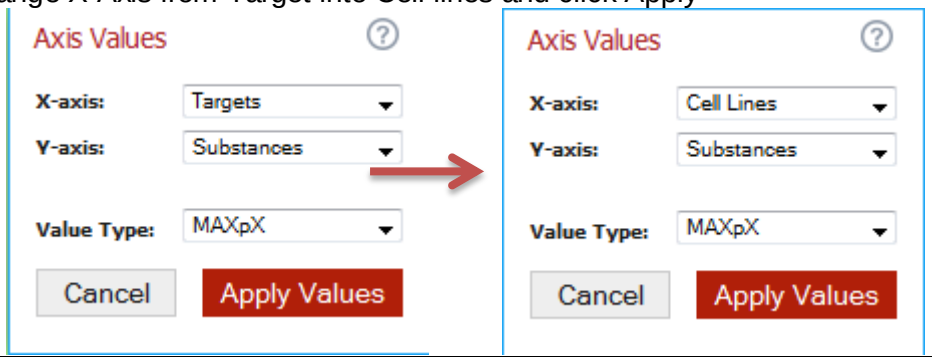


Color indicates bioactivity potency based on pX value. Number indicates pX value. (See legend Below)

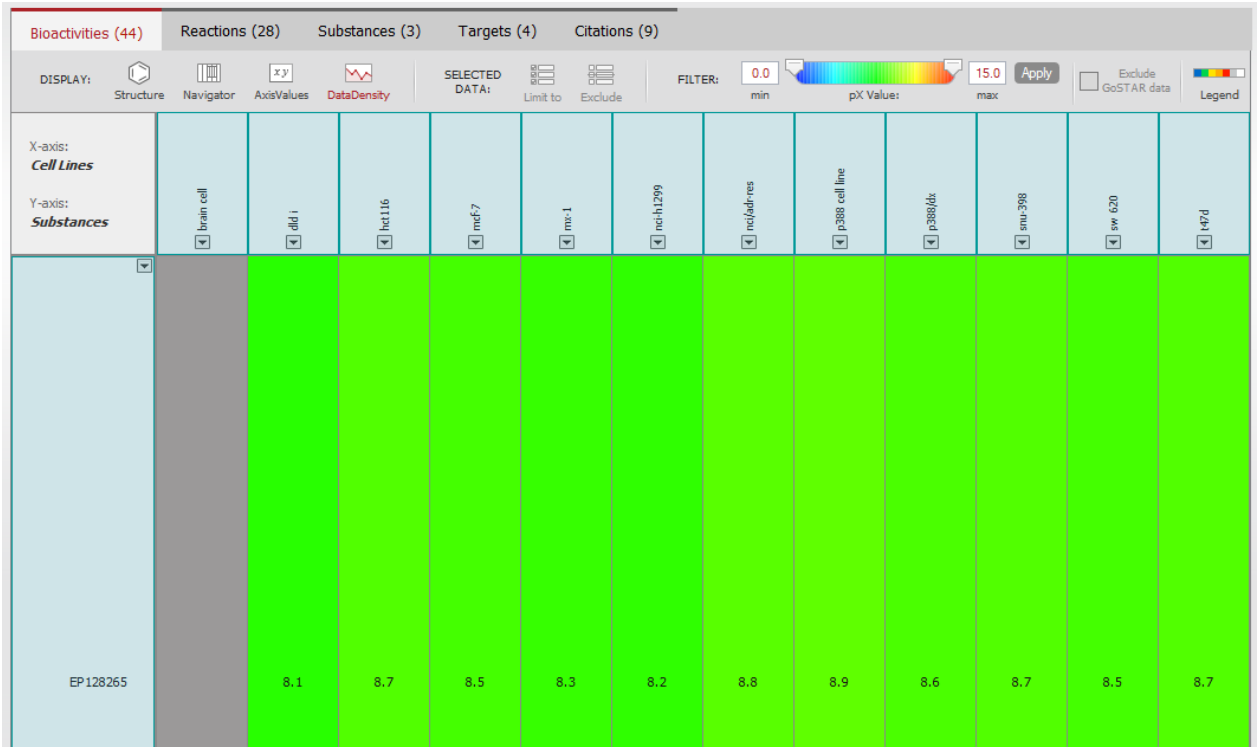


Step 6 : How to see the profile of compound 2 on Cell lines?

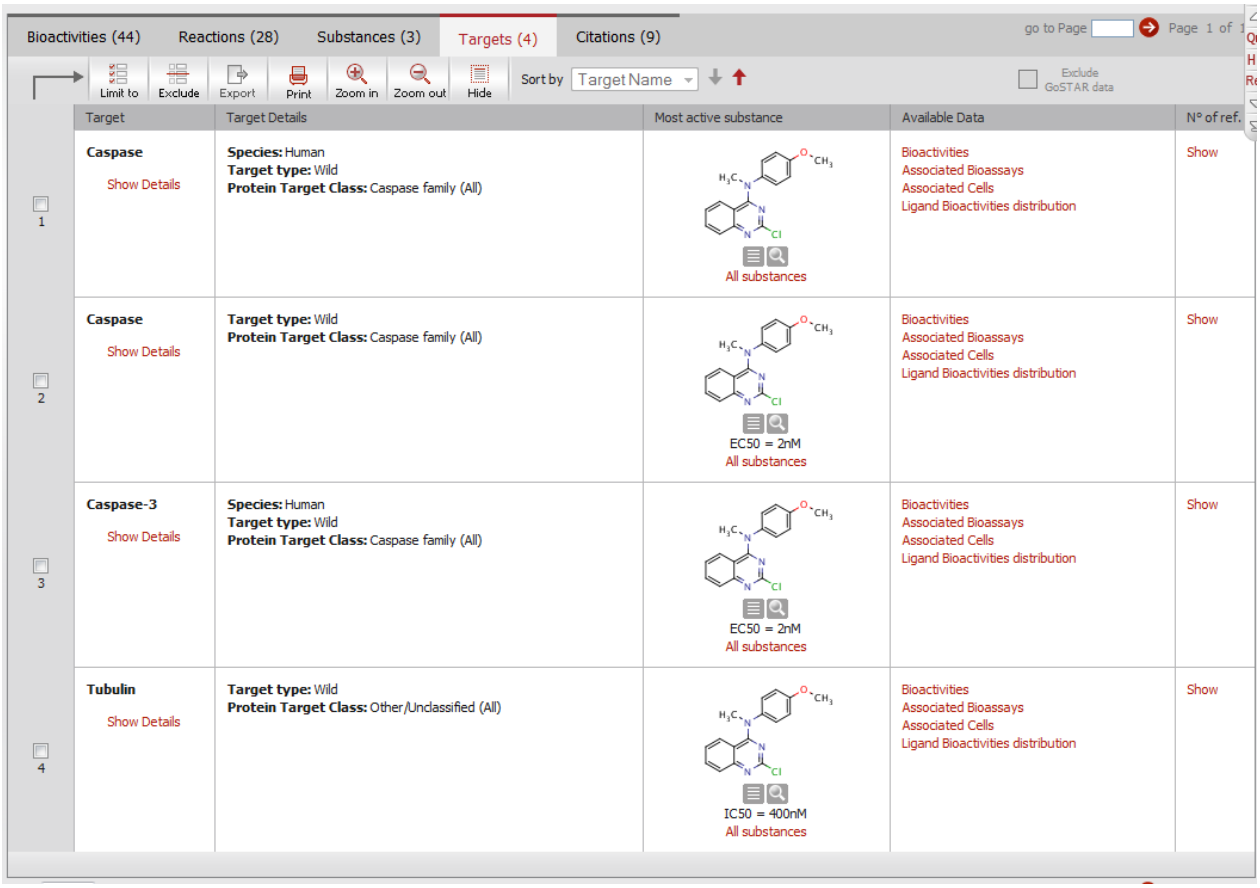
As we have seen before the compound 2 was also tested as antiproliferative agent on many cells lines how to see that using the bioactivies view?

Step	Action
1	Click on Axis Value 
2	Change X Axis from Target into Cell lines and click Apply 

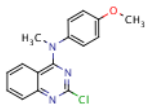
A profile on target will appear in the Bioactivities view.



Step 7 : Click the Targets Tab to have more details on targets on which this compound was tested (species etc….)

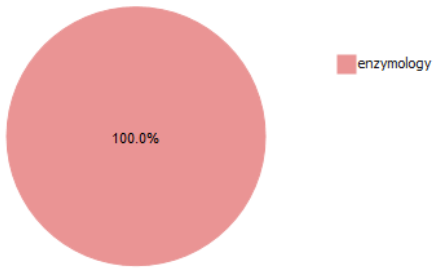


Step 8 : To know which bioassays and/or Cells lines were used to generate the corresponding bioactivities on the caspase 3 click Show details

Caspase-3 Hide Details	**Species:** Human **Target type:** Wild **Protein Target Class:** Caspase family (All)	 EC50 = 2nM All substances	Bioactivities Associated Bioassays Associated Cells Ligand Bioactivities distribution	Show

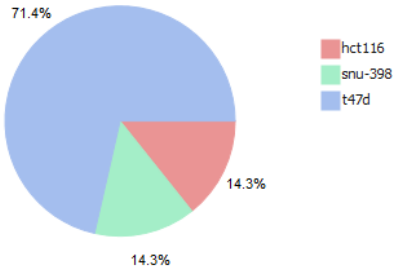
Associated Bioassays

Bioactivities distributed over Bioassays



Associated Cells

Bioactivities distributed over Cell Lines



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